```
Uploading 09769450.str

L1      STRUCTURE UPLOADED

=> s sss sam l1
SAMPLE SEARCH INITIATED 14:42:19 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -  14361 TO ITERATE

  7.0% PROCESSED    1000 ITERATIONS                          50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       280051 TO   294389
PROJECTED ANSWERS:           73816 TO    81282

L2           50 SEA SSS SAM L1

=>
Uploading 09769450b.str

L3      STRUCTURE UPLOADED

=> s sss sam l3
SAMPLE SEARCH INITIATED 14:47:47 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    592 TO ITERATE

100.0% PROCESSED     592 ITERATIONS                          39 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        10381 TO    13299
PROJECTED ANSWERS:             406 TO     1154

L4           39 SEA SSS SAM L3

=> s sss full l3
FULL SEARCH INITIATED 14:48:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  11663 TO ITERATE

100.0% PROCESSED   11663 ITERATIONS                        1047 ANSWERS
SEARCH TIME: 00.00.01

L5         1047 SEA SSS FUL L3

=> file caplus medline
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             152.15     152.36

FILE 'CAPLUS' ENTERED AT 14:48:28 ON 13 JUN 2003
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'MEDLINE' ENTERED AT 14:48:28 ON 13 JUN 2003

=> s l5
L6         199 L5

=> s l6 and kappa
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```
L7          113 L6 AND KAPPA

=> s l7 and py<= 1996
L8           58 L7 AND PY<= 1996

=> s l8 and pruritus
L9            0 L8 AND PRURITUS

=> duplicate remove l8
DUPLICATE PREFERENCE IS 'CAPLUS, MEDLINE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L8
L10          44 DUPLICATE REMOVE L8 (14 DUPLICATES REMOVED)
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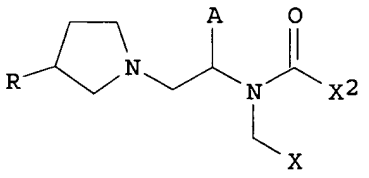
L10 ANSWER 2 OF 44 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:410432 CAPLUS
DOCUMENT NUMBER: 125:86487
TITLE: Preparation of N-[2-(1-pyrrolidinyl)-1-phenylethyl]acetamide as **kappa**-receptor agonists
INVENTOR(S): Ito, Fumitaka
PATENT ASSIGNEE(S): Pfizer Pharmaceuticals Inc., Japan
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9606078	A1	19960229	WO 1994-JP1399	19940824	<--
W: JP					
CA 2196885	AA	19960229	CA 1995-2196885	19950518	<--
CA 2196885	C	20010123			
WO 9606077	A1	19960229	WO 1995-IB374	19950518	<--
W: AU, CA, CN, CZ, FI, HU, JP, KR, MX, NO, NZ, PL, RU, US					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9523506	A1	19960314	AU 1995-23506	19950518	<--
EP 777649	A1	19970611	EP 1995-917437	19950518	
EP 777649	B1	19990714			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
JP 09510731	T2	19971028	JP 1995-529926	19950518	
JP 2935899	B2	19990816			
AT 182138	E	19990715	AT 1995-917437	19950518	
ES 2133767	T3	19990916	ES 1995-917437	19950518	
BR 9503775	A	19960416	BR 1995-3775	19950823	<--
FI 9700746	A	19970221	FI 1997-746	19970221	
US 5837720	A	19981117	US 1997-793225	19970417	

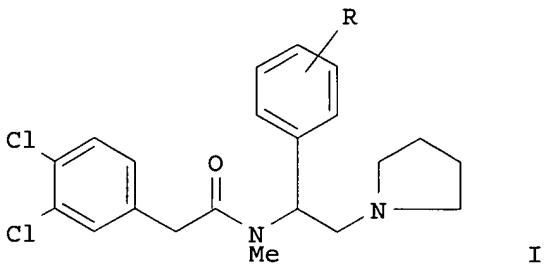
PRIORITY APPLN. INFO.: WO 1994-JP1399 A 19940824
WO 1995-IB374 W 19950518
OTHER SOURCE(S): MARPAT 125:86487
GI



I

AB The title compds. [I; R = hydrogen or hydroxy; A = (un)substituted Ph; X = (un)substituted Ph or heterocyclic, mono-, di- or tri-halomethyl, cyano, etc.; X1 = Ph, furyl, thienyl, pyridyl, thiazolyl, benzofuryl, benzothienyl, etc.], which have agonist activity toward opioid **kappa** receptors (no data) and are useful as analgesics (no data), antiinflammatory agents (no data), diuretics(no data), and neuroprotective agents (no data), are prepd. Thus, (2S,3S)-1-[2-N-(benzyloxycarbonyl)methylamino-2-phenylethyl]-3-hydroxypyrrolidine was condensed with 3,4-dichlorophenylacetyl chloride and the free base salified with HCl, producing the hydrochloride salt of N-(benzylcarbonyl)methyl-2-(3,4-dichlorophenyl)-N-[2-(3-(S)-hydroxypyrrolidin-1-yl)-1-(S)-phenylethyl]acetamide.

L10 ANSWER 15 OF 44 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 4
ACCESSION NUMBER: 1995:217334 CAPLUS
DOCUMENT NUMBER: 122:9806
TITLE: .**kappa**. Opioid Receptor Selective Affinity Labels: Electrophilic Benzeneacetamides as .**kappa**.-Selective Opioid Antagonists
AUTHOR(S): Chang, An-Chih; Takemori, Akira E.; Ojala, William H.; Gleason, William B.; Portoghese, Philip S.
CORPORATE SOURCE: College of Pharmacy, University of Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Journal of Medicinal Chemistry (**1994**), 37(26), 4490-8
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Pyrrolidinylethylacetamides I [R = 3-, 4-NCS, (E)-NHCOCH:CHCO2Me] were synthesized as .**kappa**.-selective affinity labels and evaluated for opioid activity. In smooth muscle prepns., the non-electrophilic parent compd. (+)-S-I [R = H] and the affinity labels behaved as .**kappa**. agonists in that they were potently antagonized by norbinaltorphimine (norBNI). In addn. to the high binding affinity and selectivity of I [R = 3-NCS] to .**kappa**. opioid receptors, wash studies have suggested that this involves covalent binding. In the mouse tail-flick assay, I [R = NCS] produced long-lasting antagonism of the antinociceptive effect of the .**kappa**. opioid agonist, (.+-.)-trans-2-(3,4-dichlorophenyl)-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]acetamide ((.+-.)-U50,488). In contrast, the non-electrophilic parent compd. (+)-S-I [R = H] and I [R = 3-(E)-NHCOCH:CHCO2Me] were devoid of antagonist activity in the tail-flick assay. At substantially different doses, I [R = 3-, 4-NCS] also produced antinociception in the mouse abdominal stretch assay. In addn., I [R = 3-NCS, 3-(E)-NHCOCH:CHCO2Me] had improved in vivo .**kappa**.-selectivities compared to (+)-S-I [R = H] and I [R = 4-(E)-NHCOCH:CHCO2Me]. The improved .**kappa**.-selectivities of I [R = 3-NCS, 3-(E)-NHCOCH:CHCO2Me] and the different agonist and antagonist potencies of I [R = 3-, 4-NCS] may be explained resp. by the existence of multiple .**kappa**. agonist binding sites and distinct agonist and antagonist binding sites. In view of the antagonist selectivity and the apparent irreversible binding of I [R = 3-NCS] to .**kappa**. receptors, it may serve as a useful pharmacol. or biochem. tool to investigate .**kappa**. opioid receptors.